UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/612,929	04/30/96	HOLMES S	P50186-2

18M1/0123

JEFFREY A. SUTTON
SMITHKLINE BEECHAM CORPORATION
CORPORATE INTELLECTUAL PROPERTY UW2220
PO BOX 1539
KING OF PRUSSIA PA 19406-0939

EXAMINER	
HUFF,S	

ART UNIT	PAPER NUMBER
1806	

DATE MAILED: 01/23/98

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 08/612,929	Applicant(s) Holmes et al
	Examiner Sheela J. Huff	Group Art Unit 1806

☒ Responsive to communication(s) filed on *Nov 10, 1997* .

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-11, 14-18, and 30-40* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-11, 14-18, and 30-40* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Response to Amendment

1.The amendment filed on 11/10/97 has been considered. Applicant's arguments are deemed to be persuasive-in-part.

Claims 12-13 and 19-29 have been cancelled.

Claims 39-40 have been added.

2.The rejection of claims 3 and 37-38 under 35 U.S.C. 112, first paragraph, is withdrawn in view of applicant's statement.

3.The rejection of claim 30 under 35 U.S.C. 112, first paragraph, is withdrawn in view of applicant's amendment.

4.The rejections under 35 U.S.C. 112, second paragraph, are withdrawn in view of applicant's arguments and amendments.

5.The rejection of claims 1, 8-9, 11 and 17 under 35 U.S.C. 102(a) as being anticipated by WO 93/04173 (3/4/93) is withdrawn in view of applicant's amendment and arguments.

6.The rejection of claims 1-4, 14-17, 31-34 and 36 under 35 U.S.C. 102(a) as being anticipated by WO 93/17106 (9/2/93) is withdrawn in view of applicant's arguments.

7.The rejection of claims 1-2, 4, 8-9, 11, 14 and 16-17 under 35 U.S.C. 102(b) as being anticipated by EP 327000 is withdrawn in view of applicant's arguments.

8.The rejection of claim 11 under 35 U.S.C. 102(b) as being anticipated by Loh et al, Nature vol. 276 p. 785 (1978) is withdrawn in view of applicant's arguments.

9.The rejection of claims 1-4, 7 and 10 under 35 U.S.C. 102(b) as being anticipated by Perfetti et al. Molec. Immunol. vol. 287 p. 505 (1991) is withdrawn in view of applicant's amendment.

10.The rejection of claim 33 under 35 U.S.C. 102(b) as being anticipated by Ramanathan *et al* (WO/91/09059) is withdrawn in view of applicant's arguments.

11.The rejection of claim 33 under 35 U.S.C. 102(b) as being anticipated by Chretien *et al.* J. Immunol. Methods vol. 117 p. 67 (1991) is withdrawn in view of applicant's arguments.

Response to Arguments

Double Patenting

12. A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

13. Claims 1-11, 14-17, 30 and 32-38 remain provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-11, 14-17, 30 and 32-38 of copending Application No. 08/483636. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented. The reasons for this rejection are of record in paper no. 10, mailed 5/9/97.

Applicant will address this issue at time of allowance.

Claim Rejections - 35 USC § 112

14. Claims 17-18 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The reasons for this rejection are of record in paper no. 10, mailed 5/9/97. Since applicant has amended claim 1 to indicate 6 CDRs, the rejection pertaining to full complement of CDRs is withdrawn. However, the rejection with respect to unspecified order and fused to any framework is maintained because claim 1 still reads on CDRs in an unspecified order and using no or any framework.

Applicant cites pages 1, 21-23 and 32-37. While these pages do show in vitro assays and one pharmacokinetics study, these passages do not demonstrate that the antibodies have the same effect in vivo as they do in vitro. Applicant further argues that it is well established that in vitro is enough to support in vivo claims if there is reasonable

correlation between in vitro data and in vivo. This is true. However, there is no objective evidence of record to that the in vitro assays in the specification are predictive of in vivo use.

15. Claims 1-4 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for fusion proteins containing the full complement of CDRs, does not reasonably provide enablement for fusion proteins containing CDRs in an unspecified order. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The reasons for this rejection are of record in paper no. 10, mailed 5/9/97.

Applicant believes that the amendments to the claims overcome this rejection. Since applicant has amended claim 1 to indicate 6 CDRs, the rejection pertaining to full complement of CDRs is withdrawn. However, the rejection with respect to unspecified order and fused to any framework is maintained because claim 1 still reads on CDRs in an unspecified order and using no or any framework.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

16. Claim 30 remains rejected under 35 U.S.C. 102(b) as being anticipated by JP-327725. Claim 33 has been withdrawn from this rejection. The reasons for this rejection are of record in paper no. 10, mailed 5/9/97.

Applicant argues that the reference does not teach diagnostic methods for identifying patients. The claim is not directed to diagnosing for the identification but is directed to detecting excess IgGE.

Claim Rejections - 35 USC § 102/103

17. Claim 32 is rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Ramanathan *et al* (WO91/09059) or JP-327725 or Cretien J. Immunol. Methods vol. 117 p. 67 (1991). The reasons for this rejection are of record in paper no. 10, mailed 5/9/97. Note claim 1 is withdrawn from this rejection and made into a 103--see below.

Applicant argues that the dissociation constant is not inherent. There is no dissociation mentioned in claim 32.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

18. The factual inquiries set forth in *Graham v. John Deere Co.*, 148 USPQ 459, that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or unobviousness.

19. Claim 1 remains rejected under 35 U.S.C. 103(a) as obvious over Ramanathan *et al* (WO91/09059) or JP-327725 or Cretien J. Immunol. Methods vol. 117 p. 67 (1991). The reasons for this rejection are of record in paper no. 10, mailed 5/9/97.

Applicant states that arguments for this rejection are that same as those to the rejections under 102. However, The rejection was initially a 102/103 rejection and now the 102 is withdrawn. Applicant did not respond to the rejection under 103. To the extent that applicant questions the range of the dissociation constant, applicant is directed to Harlow and Lane, "antibodies: A Laboratory Manual" 1988 p. 27, which states that dissociation constant range from 10^5 mol^{-1} to above 10^{12} mol^{-1}.

20. Claims 1-2, 4, 14-17 and 30-34 and 36 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Queen *et al* (WO 90/07861) in view of Abrams *et al* US 5041381, Chretien *et al* J. Immunol. Methods vol. 117 p. 67 (1991) and Curtis *et al* US 5108910. The reasons for this rejection are of record in paper no. 10, mailed 5/9/97.

Applicant against refers to the dissociation constant. Applicant's arguments have been addressed above.

21. Claim 31 remains rejected under 35 U.S.C. 103(a) as being unpatentable over WO 91/09059 or Chretien *et al* J. Immunol. Methods vol. 117 p. 67 (1991).

Both references disclose screening procedures (ELISA) for anti-IL-4 antibodies (p. 16 of WO and p. 69 of Chreiten et al). The reasons for this rejection are of record in paper no. 10, mailed 5/9/97.

Applicant has not provided any arguments to this rejection.

New Grounds of Rejection

Claim Rejections - 35 USC § 103

22. Claim 1 ~~and 40~~ are rejected under 35 U.S.C. 103(a) as obvious over Loh et al nature vol. 276 p. 785 (1978).

This reference discloses the amino acid sequence of light chains are comprising amino acid sequences comprising Seq ID No 16 and 18 of the instant invention (Figure 2).

The invention of claim 1 is characterized as a fusion protein. However, given the lack of specified structural elements in the claims to distinguish the claimed fusion proteins from those that would be produced by hybridomas as disclosed in the cited references. The claimed fusion protein is deemed to be the same as the monoclonal antibodies taught in the prior art.

Although the reference appears to disclose the same product claimed by applicants, the reference does not disclose the products <u>produced</u> by the claimed process. However

the purification of production of a product by a particular process does not impart novelty to a product when the product is taught by the prior art. This is particularly true when the properties of the product are not changed by the process in an unexpected manner.

See In re Thorpe, 227 USPQ 964 (CAFC 1985); In re Marosi, 218 USPQ 289, 292-293 (CAFC 1983); In re Brown, 173 USPQ 685 (CCPA 1972).

Therefore even if a particular process used to prepare a product is novel and unobvious over the prior art, the product per se, even when limited to the particular process, is unpatentable over the same product taught by the prior art.

See In re King, 107 F. 2d 618, 620, 43 USPQ 400, 402 (CCPA 1939); In re Merz, 97 F. 2d 599, 601, 38 USPQ 143-145 (CCPA 1938); In re Bergy, 563 F. 2d 1031, 1035, 195 USPQ 344, 348 (CCPA 1977) vacated 438 US 902 (1978); and United States v. Ciba-Geigy Corp, 508 F. Supp. 1157, 1171, 211 USPQ 529, 543 (DNJ 1979).

Even if the prior art antibodies are not identical to those instantly claimed, given the teaching of the prior art specifically characterizing the anti-IL-4 antibodies in combination with conventional hybridoma methods if would have been *prima facie* obvious to produce similar antibodies having the same specificity and function. One of ordinary skill in the art would have expected to obtain antibodies having the claimed affinity, since affinity constants for antigen-antibody binding within the range of 10^5 mol^{-1} to greater than 10^{10} mol^{-1} are commonly observed. It would have been *prima facie* obvious to apply well established immunoglobulin gene cloning and expression methods to produce fusion

proteins such as chimeric antibodies, having variable regions of the antibodies suggested by the prior art.

Double Patenting

23. The non-statutory double patenting rejection, whether of the obviousness-type or non-obviousness-type, is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent. *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); and *In re Goodman*, 29 USPQ2d 2010 (Fed. Cir. 1993).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(b) and (c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.78(d).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

24. Claims 1 and 39 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 10 of copending Application No. .08/483636 Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims in the instant invention require two sequences and the claims in related case does not have this limitation.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

25. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. US 5597710 Dalle et al and Dalie et al US 5705154

26. No claim is allowed.

27. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

28. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheela J. Huff whose telephone number is (703) 305-7866. The examiner can normally be reached on Monday-Thursday from 6:30am to 3:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lila Feisee, can be reached on (703)308-2731. The FAX phone number for this Group is (703)308-4242.

Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [**lila.feisee@uspto.gov**].

All Internet e-mail communications will be made of record in the application file. **PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122.** This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Sheela J. Huff
January 20, 1998

Sheela J. Huff
Primary Examiner